

## AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 5, line 14 with the following rewritten paragraph:

**FIGURE 4A, 4B, 4C, 4D, 4E, 4F, 4G, 4H, and 4I.** Cytotoxic activity and EBV latent antigen specificity of T cell subsets. ~~The left column (A-C)~~ FIGURE A-C shows the CD8 vs. CD4 FACS stainings of three PBMC responder populations: (A) CD2<sup>+</sup>PBMC, (B) CD8<sup>-</sup>CD2<sup>+</sup>PBMC and (C) CD4<sup>-</sup>CD2<sup>+</sup>PBMC. ~~The middle column (D-F)~~ FIGURE D-F displays the observed lysis of autologous LCL (LCL-JT; solid circles) and T2 cells (T2; open circles) by these responders. ~~In the right column (G-I)~~ FIGURE G-I depicts the EBV latent antigen specificity of the three responder populations ~~was~~ investigated in an ELISPOT assay (E1: vvEBNA-1ΔGA, E2: vvEBNA2, E3B: vvEBNA3B, E3C: vvEBNA3C, L1: vvLMP1, L2a: vvLMP2A, B1: vvBMLF1, LCL: LCL-JT).

Please replace the paragraph beginning on page 5, line 23 with the following rewritten paragraph:

**FIGURE 5A, 5B, 5C, 5D, 5E, and 5F.** HLA-DR restriction and EBNA-1 recognition by CTL subsets. The effectors, as shown on the top, were either CD2<sup>+</sup>PBMC (A,D), CD8<sup>-</sup>CD2<sup>+</sup>PBMC (B, E) or CD4<sup>-</sup>CD2<sup>+</sup>PBMC (C,F). ~~The top row (A-C)~~ FIGURE 5 A-C shows the cytolysis of autologous B-LCL (LCL-JT) in the presence (open circles, dotted line) or absence (solid circles) of 5 µg/ml L243,  $\alpha$ HLA-DR antibody (LCL-JT + L243). T2 cells (solid triangles) were used as a control. ~~The bottom row (D-F)~~ FIGURE 5 D-F shows lytic activity against autologous B-LCL (LCL-JT; open triangles) in comparison to autologous DCs pulsed with *E. coli* derived control protein (eControl; solid circles), *E. coli* derived EBNA-1 protein (eEBNA-1; open circles) or baculovirus/insect cell derived EBNA-1 protein (bEBNA-1; solid triangles).

Please replace the paragraph beginning on page 6, line 21 with the following rewritten paragraph:

**FIGURE 8A-C and 8B.** EBNA-1-specific responses can be detected at very low doses of antigen. A recombinant EBNA-1 protein or control proliferating cell nuclear antigen (PCNA)

protein was eluted from *E. coli* expressing vectors. **A.** Proteins were dialyzed overnight and tested for purity with SDS PAGE. The recovered rEBNA-1 protein was tested for specificity by Western blot using an anti-EBNA antibody MAB8173. The antibody AD1.1.10[.] recognizes a histidine tag which is contained in the rEBNA-1 protein. **B.** vvEBNA-1ΔGA-infected DCs were used to expand CD4<sup>+</sup> T cells in a one week culture. The expanded T cells were restimulated using DCs pulsed with the indicated concentration of rEBNA-1 protein or rPCNA control protein and read-out with ELSIPOT. The rEBNA-1 protein was added to the DCs during the maturation phase (day 6-8) of the DC culture. **C.** ~~The inset~~ This graph shows the ELISpot results of CD4<sup>+</sup> T cells expanded with vvEBNA-1ΔGA-infected DCs for one week and restimulated with either vvEBNA-1ΔGA-infected DCs or vvTK<sup>-</sup> control.

Please replace the paragraph beginning on page 51, line 12 with the following rewritten paragraph:

The experiments in Figure 7 used vaccinia vectors both to expand the EBNA-1-specific cells for one week and for restimulation in the ELISpot assay for one day. Therefore, we then tested the efficacy of purified EBNA-1 protein as antigen in the ELISpot assay. A recombinant EBNA-1 protein consisting of the amino acids 458-641 of the EBNA-1 sequence or rPCNA, as a control protein, were extracted from transformed *E. coli* cultures after IPTG induction. The extract was dialyzed overnight against PBS and was checked for purity and specificity by SDS PAGE and Western blot (Figure 8A). These proteins were pulsed onto DCs in varying concentrations and used to read-out IFN $\gamma$  ELISpots after a one week expansion using vvEBNA-1ΔGA-infected DCs. Figure 8B shows the dose response curve seen with the titration of rEBNA-1 protein as compared to the PCNA control. The inset graph in Figure 8C compares the response of vvEBNA-1ΔGA expanded cells restimulated with vvTK<sup>-</sup> or vvEBNA-1ΔGA. A dosage of only 1  $\mu$ g/ml of rEBNA-1 protein pulsed onto DCs gives a response that is comparable to that of the recombinant vaccinia EBNA-1. This result demonstrates that EBNA-1-specific T<sub>H</sub>1 cells are capable of responding to very low doses of EBNA-1.